Remarks

Claims 32 and 34-44 and 46-50 are pending.

Applicants also acknowledge that Claims 32 and 35-38 have been allowed and thank the Examiner for indicating as much.

Rejection Under 35 U.S.C. § 102

1. Claims 47-49 were rejected under 35 U.S.C. § 102(e), as being anticipated by McCaslin et al. (5,614,390). Applicants respectfully traverse this rejection.

McCaslin et al. discloses oligonucleotides for use as amplification primers and assay probes for species-specific detection and identification of *Mycobacterium kansasii* (see McCaslin et al. column 3, lines 44-46). The primers described by McCaslin et al. were designed to species-specifically amplify a target in both typical and atypical strains of *M. kansasii* (see McCaslin et al. column 3, lines 34-37).

The passages of McCaslin et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

Claim 47, as well as claims 48-49 that depend from Claim 47, are drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary

portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4); (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5); and (3) that the set of primers has 3 or more primers (see claim 47, lines 5-6). It is important to note that each of the 3 or more primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 2, lines 11-14) that the teachings of McCaslin et al. anticipate the limitations of the claims. For support, the Office Action cites sections of McCaslin et al. that describe the use of primers designed for species-specific detection and identification of *Mycobacterium kansasii*. Applicants first assert that the Office Action fails to specifically address each and every limitation of the claims. In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden. In particular, the Examiner has failed to address or direct the Applicants attention to portions of McCaslin et al. that disclose the above outlined limitations (1) and (2). Specifically, the Examiner has failed to address or direct the Applicants attention to portions of McCaslin et al. that disclose a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, (1) wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, and (2) wherein all of the primers in the set of primers are complementary to the same strand of the target sequence. Applicants submit that it would not be possible to point to such a description, as McCaslin et al. fails to teach these elements.

a. With regard to limitation (1) "wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target" there is no discussion, whatsoever, within the current Office Action. Nowhere, within the four corners of the current Office Action, is such a limitation addressed. In the interest of being thorough, Applicants wish to address the limitation, despite the Office Action's silence as to this limitation.

Claim 47 is drawn to a kit that comprises, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, line 3-5). In other words, each of the primers in the primer set hybridize to a different portion of the hybridization target.

McCaslin et al. fails to disclose such a limitation. As described above, McCaslin et al. discloses oligonucleotides for use as amplification primers and assay probes for species-specific detection and identification of *Mycobacterium kansasii* (see McCaslin et al. column 3, lines 44-46). The primers disclosed by McCaslin et al. are specifically set forth in column 4, lines 56-67, Table 1, and column 5, lines 1-10. Of note is that this is the same portion of McCaslin et al. cited in the Office Action. The primers disclosed by McCaslin et al. are overlapping of one another, and overlapping over the portions of the hybridization target sequence (see column 4, lines 39-41 as well as comparing the sequences of the target binding sequences (italicized) in Table 1). In other words, the each of the primers in the primer set disclosed by McCaslin et al. do not hybridize to a different portion of the hybridization target.

As such, the cited passage of McCaslin et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target. Because McCaslin et al. fails to disclose every feature of the claimed kits, McCaslin et al. fails to anticipate claims 47-49.

b. With regard to limitation (2) "wherein all of the primers in the set of primers are complementary to the same strand of the target sequence" the Office Action presents two questions (a) what is meant by the same strand of the target sequence and (b) what is the definition regarding a set of primers. First Applicants submit that "the same strand of the target sequence" does not include the complementary strand of the target sequence. This is described at least on page 34, lines 25-31 of the application, where one of the amplification methods using a set of primers where all of the primers are complementary to the same strand of the target sequence is described. Specifically, it is provided that when a set of primers where all of the

primers are complementary to the same strand of the target sequence are used, only one of the strands of the target sequence is replicated. This is due to the fact that the primers do not hybridize to the complementary strand. One of skill in the art would understand this to mean that the primers of the primer set only bind one of the strands, not both strands.

McCaslin et al. fails to disclose such a limitation. As described above, McCaslin et al. discloses oligonucleotides for use as amplification primers and assay probes for species-specific detection and identification of *Mycobacterium kansasii* (see McCaslin et al. column 3, lines 44-46). The primers disclosed by McCaslin et al. are specifically set forth in column 4, lines 56-67, Table 1, and column 5, lines 1-10. Of note is that this is the same portion of McCaslin et al. cited in the Office Action. The primers disclosed by McCaslin et al. are specifically designed to bind to both strands of a double stranded template. This can be inferred as the method of amplification for which the primers are used is a PCR amplification reaction (see column 4, lines 4-5). One of skill in the art would clearly recognize that a PCR amplification reaction requires primers that bind to both the sense and antisense (complementary) strands. This is not the same as the claimed primers that all of the primers in the set of primers are complementary to the same strand of the target sequence.

As such, the cited passages of McCaslin et al. fail to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence. Because McCaslin et al. fails to disclose every feature of the claimed kits, McCaslin et al. fails to anticipate claims 47-49.

Therefore, Applicants submit that the Examiner has not met her burden of providing specific reference to where McCaslin et al. discloses each and every element of the claims and furthermore, McCaslin et al. fails to disclose each and every element of the claims. Because McCaslin et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

2. Claim 47 was rejected under 35 U.S.C. § 102(e), as being anticipated by Walker et al. (5,736,365). Applicants respectfully traverse this rejection.

Walker et al. discloses methods for simultaneous amplification of multiple target sequences by sequence specific hybridization of primers, particularly by SDA (multiplex SDA) (see Walker et al. column 4, lines 34-36). The methods use a single pair of amplification primers or a single SDA amplification primer to coamplify the multiple target sequences (see Walker et al. column 4, lines 36-39).

The passages of Walker et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

Claim 47 is drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, claim 47 requires the set of primers to have specific attributes and abilities. In particular, claim 47 requires: (1) that the each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4); (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5); and (3) that the set of primers has 3 or more primers (see claim 47, lines 5-6). It is important to note that each of the 3 or more primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 3, lines 5-9) that the teachings of Walker et al. anticipate the limitations of the claims. For support, the Office Action cites sections of Walker et al. that describe packaging the primers and/probes for performing adapter-mediated multiplex amplification of the IS6110 insertion element of *Mycobacterium tuberculosis* (M.tb) and the 16S ribosomal gene of *Mycobacterium tuberculosis* complexes. Specifically, the Office Action cites column 10, lines 54-57 (page 3, lines 5-6) where Walker et al. provides that the primers and/or probes for performing the assay methods of the invention may be packaged in the form of a kit. The Office Action is correct in that Walker et al. does disclose three different type of primers, namely an amplification primer, an adapter primer and a bumper primer. However, the Office Action fails to note that these three types of primers when used to perform the assay methods of the invention of Walker et al. are not complementary to the same strand of the target sequence. For example, Figure 1 of Walker et al. illustrates the method of the Walker et al. invention. As illustrated in Figure 1, the amplification primer (Stb and the bumper primer (Btb1) bind the same strand (see description above that same strand does not include the complementary strand). Once the primes are extended. Once the first strand is amplified, the second bumper primer (Btb2) and the adapter primer (Atb) bind the amplified strand (complement) of the original target strand. Therefore, at most, 2 primers bind the same strand of the target sequence. Thus, even if the primers of Walker et al. were in a kit, the kit would not comprisea set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

As such, the cited passage of Walker et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. Because

Walkr et al. fails to disclose every feature of the claimed kits, Walker et al. fails to anticipate claim 47.

As such, Applicants submit that Walker et al. fails to disclose each and every element of the claims. Because Walker et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 103

1. Claim 50 was rejected under 35 U.S.C. § 103(a), as being unpatentable over McCaslin et al. (5,614,390) as applied to claims 47-49 or over Walker et al. (5,736,365) as applied to claim 47 above, and in further view of Blanco et al. (Journal of Biological Chemistry, 1989, Vol. 264(15), pg. 8935-40). Applicants respectfully traverse this rejection.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

With regard to the subject matter of Claim 50, Applicants first note that Claim 50 depends from Claim 47 and by definition encompasses all the elements of Claim 47. This is important because the Office Action applies McCaslin et al. and Walker et al. in the same way and for the same disclosures for which McCaslin et al. and Walker et al. were applied in the rejection of claims 47-49 and 47, respectively, under 35 U.S.C. § 102(e) addressed above.

Concerning McCaslin et al., McCaslin et al. discloses oligonucleotides for use as amplification primers and assay probes for species-specific detection and identification of *Mycobacterium kansasii* (see McCaslin et al. column 3, lines 44-46). The primers described by McCaslin et al. were designed to species-specifically amplify a target in both typical and atypical strains of *M. kansasii* (see McCaslin et al. column 3, lines 34-37).

The Office Action alleges (page 2, lines 11-14) that the teachings of McCaslin et al. anticipate the limitations of claims 47-49. For support, the Office Action cites sections of

McCaslin et al. that describe the use of primers designed for species-specific detection and identification of *Mycobacterium kansasii*. Applicants first assert that the Office Action fails to specifically address each and every limitation of the claims. In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden. In particular, the Examiner has failed to address or direct the Applicants attention to portions of McCaslin et al. that disclose the above outlined limitations (1) and (2). Specifically, the Examiner has failed to address or direct the Applicants attention to portions of McCaslin et al. that disclose a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, (1) wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, and (2) wherein all of the primers in the set of primers are complementary to the same strand of the target sequence. Applicants submit that it would not be possible to point to such a description, as McCaslin et al. fails to teach these elements.

a. With regard to limitation (1) "wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target" there is no discussion, whatsoever, within the current Office Action. Nowhere, within the four corners of the current Office Action, is such a limitation addressed. In the interest of being thorough, Applicants wish to address the limitation, despite the Office Action's silence as to this limitation.
Claim 47 is drawn to a kit that comprises, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, line 3-5). In other words, each of the primers in the primer set hybridize to a different portion of the hybridization target.

McCaslin et al. fails to disclose such a limitation. As described above, McCaslin et al. discloses oligonucleotides for use as amplification primers and assay probes for species-specific detection and identification of *Mycobacterium kansasii* (see McCaslin et al. column 3, lines 44-46). The primers disclosed by McCaslin et al. are specifically set forth in column 4, lines 56-67, Table 1, and column 5, lines 1-10. Of note is that this is the same portion of McCaslin et al. cited

in the Office Action. The primers disclosed by McCaslin et al. are overlapping of one another, and overlapping over the portions of the hybridization target sequence (see column 4, lines 39-41 as well as comparing the sequences of the target binding sequences (italicized) in Table 1). In other words, the each of the primers in the primer set disclosed by McCaslin et al. do not hybridize to a different portion of the hybridization target.

As such, the cited passage of McCaslin et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target.

b. With regard to limitation (2) "wherein all of the primers in the set of primers are complementary to the same strand of the target sequence" the Office Action presents two questions (a) what is meant by the same strand of the target sequence and (b) what is the definition regarding a set of primers. First Applicants submit that "the same strand of the target sequence" does not include the complementary strand of the target sequence. This is described at least on page 34, lines 25-31 of the application, where one of the amplification methods using a set of primers where all of the primers are complementary to the same strand of the target sequence is described. Specifically, it is provided that when a set of primers where all of the primers are complementary to the same strand of the target sequence are used, only one of the strands of the target sequence is replicated. This is due to the fact that the primers do not hybridize to the complementary strand. One of skill in the art would understand this to mean that the primers of the primer set only bind one of the strands, not both strands.

McCaslin et al. fails to disclose such a limitation. As described above, McCaslin et al. discloses oligonucleotides for use as amplification primers and assay probes for species-specific detection and identification of *Mycobacterium kansasii* (see McCaslin et al. column 3, lines 44-46). The primers disclosed by McCaslin et al. are specifically set forth in column 4, lines 56-67, Table 1, and column 5, lines 1-10. Of note is that this is the same portion of McCaslin et al. cited in the Office Action. The primers disclosed by McCaslin et al. are specifically designed to bind to both strands of a double stranded template. This can be inferred as the method of

amplification for which the primers are used is a PCR amplification reaction (see column 4, lines 4-5). One of skill in the art would clearly recognize that a PCR amplification reaction requires primers that bind to both the sense and antisense (complementary) strands. This is not the same as the claimed primers that all of the primers in the set of primers are complementary to the same strand of the target sequence.

As such, the cited passages of McCaslin et al. fail to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence.

Concerning Walker et al., Walker et al. discloses methods for simultaneous amplification of multiple target sequences by sequence specific hybridization of primers, particularly by SDA (multiplex SDA) (see Walker et al. column 4, lines 34-36). The methods use a single pair of amplification primers or a single SDA amplification primer to coamplify the multiple target sequences (see Walker et al. column 4, lines 36-39).

The Office Action alleges (page 3, lines 5-9) that the teachings of Walker et al. anticipate the limitations of the claims. For support, the Office Action cites sections of Walker et al. that describe packaging the primers and/probes for performing adapter-mediated multiplex amplification of the IS6110 insertion element of *Mycobacterium tuberculosis* (M.tb) and the 16S ribosomal gene of *Mycobacterium tuberculosis* complexes. Specifically, the Office Action cites column 10, lines 54-57 (page 3, lines 5-6) where Walker et al. provides that the primers and/or probes for performing the assay methods of the invention may be packaged in the form of a kit. The Office Action is correct in that Walker et al. does disclose three different type of primers, namely an amplification primer, an adapter primer and a bumper primer. However, the Office Action fails to note that these three types of primers when used to perform the assay methods of the invention of Walker et al. are not complementary to the same strand of the target sequence. For example, Figure 1 of Walker et al. illustrates the method of the Walker et al. invention. As illustrated in Figure 1, the amplification primer (Stb and the bumper primer (Btb1) bind the same strand (see description above that same strand does not include the complementary strand). Once the primes are extended. Once the first strand is amplified, the second bumper primer (Btb2) and

the adapter primer (Atb) bind the amplified strand (complement) of the original target strand. Therefore, at most, 2 primers bind the same strand of the target sequence. Thus, even if the primers of Walker et al. were in a kit, the kit would not comprisea set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

As such, the cited passage of Walker et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers.

Blanco et al. fails to supplement the elements missing from McCaslin et al. and Walker et al. Blanco et al. was cited for its alleged disclosure that phage vphi 29 DNA polymerase is highly processive in the absence of any accessory protein and is able to produce strand displacement coupled to the polymerization process. The Examiner has not relied on Blanco et al. nor directed the Applicants to any portions of Blanco et al. that address a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers, which Applicants submit would not be possible, as Blanco et al. fails to teach these elements.

As such, Applicants submit that neither Walker et al., McCaslin et al., Walker et al. nor Blanco et al. either alone or in combination disclose or suggest each and every element of the claims. Accordingly, neither Walker et al., McCaslin et al., Walker et al. nor Blanco et al. either

alone or in combination make obvious claim 50. Applicants respectfully request withdrawal of this rejection.

2. Claims 34 and 39-44 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Hartley et al. (5,043,272) in view of Van Gelder et al. (5,891,636). Applicants respectfully traverse this rejection.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

a. Hartley et al. discloses a process for the amplification of a nucleic acid template in a sample, which process comprises synthesis of nucleic acid sequences in a randomly primed, but template dependent manner. The method, described as Random Priming Amplification (RPA) employs the use of random primers (see Hartley et al. column 2, lines 54 – column 3, line 2). The primers disclosed by Hartley et al. contain sequences not designed to be directed to a specific sequence in the nucleic acid sample to be amplified (see Hartley et al. column 5, lines 14).

Claims 34 and 39-45 that depend from Claim 34, are drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, the claims require that the primers have random nucleotide sequences. In addition to the random nucleotide sequences, the primers comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence.

In other words, within the set of primers in the kit, each primer has a constant portion that is the same as each and every other primer in the set. (see Claim 34 above, lines 5-7).

The passages of Hartley et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. In fact, the Office Action now admits on page 6, line 10, that Hartley et al. does not disclose the random primer comprising a constant portion. The Office Action now attempts to supplement the lack of such a teaching in Hartley et al. by citing portions of Van Gelder et al.

Van Gelder et al. discloses processes of amplifying at least one sequence in a collection of nucleic acids sequences through the use of "primer complexes" (see column 2, lines 34-52). The primer complexes refer to an oligonucleotide having two components: (1) a primer and (2) a specifically oriented RNA polymerase promoter region (see column 6, lines 62-65).

The Office Action alleges on page 6, lines 11-14, that the invention of Van Gelder et al., can be provided in a kit for a variety of uses and that the kit may contain random primers linked to a promoter reactive with the RNA polymerase. Specifically, the Office Action cites column 3, lines 43-44 as well as column 10, lines 46-57 in support of its allegation. Applicants first note that the kits of Van Gelder et al. are noted to typically comprise, other than instructions, reverse transcriptase, RNA polymerase, and nucleotides which may be labeled (see column 3, lines 44-48). Of note is that there is no mention of a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase as required by the current claims under rejection. Applicants submit that this is purposely omitted from the kits of Van Gelder et al. because such enzymes are inconsistent with the methods taught by Van Gelder et al. The method of Van Gelder et al. is set forth in Figure 1. In essence, the method of Van Gelder et al. begins with the synthesis of cDNA by treating mRNA from the sample of interest (mRNA is therefore the "target") with the disclosed primer complexes. This step is required in each of the embodiments disclosed by Van Gelder et al. (see Summary of the Invention, column 2, line 33 - column 3, line 43). In other words, the primer complexes bind to mRNA and are extended with a reverse transcriptase.

The Office Action alleges on page 6, lines 15-21 that one of skill in the art would have been motivated to include the primer complexes disclosed by Van Gelder et al. in the kit of Hartley et al, based on the statement in Van Gelder et al. that the kit containing the primer complexes can have a variety of uses. Applicants submit that the Office Action has inappropriately over reached on the assertion of Van Gelder et al. that the kit containing the primer complexes can have a variety of uses. While it may be true that the kits of Van Gelder et al. can be used in a variety of uses, the fact still remains that the primer complexes of Van Gelder et al. are used only in a reverse transcription reaction to produce cDNA from mRNA. Nowhere in Van Gelder et al. are the primer complexes used in a reaction with a DNA polymerase. In fact, nowhere in Van Gelder et al. is the use of the primer complexes in a DNA amplification reaction described. The primer complexes disclosed by Van Gelder et al. are specifically designed for the reverse transcription reaction outlined above (see above and Van Gelder et al., Summary of the Invention, column 2, line 33 - column 3, line 43). As such, there is no link to placing the primer complexes of Van Gelder et al. in a kit with a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase.

Thus, Hartley et al. or Van Gelder et al., either alone or in combination, fail to disclose or suggest each and every element of claims 34 and 39-44. Accordingly, Hartley et al. or Van Gelder et al. do not make obvious claims 34 and 39-44. Applicants respectfully request withdrawal of this rejection.

b. Applicants further assert that if it is the Examiner's contention that the general idea allegedly taught by Van Gelder et al., namely a primer with a random and a constant portion, can be extracted from Van Gelder et al., and modified and applied to the primers and kits of Hartley et al., such an assertion is completely impermissible hindsight.

It is not enough to combine cited references with unspecified knowledge in the art without some objective reason to do so. Rather, to make this combination without evidence of such knowledge or the suggestion, teaching or motivation to combine is an impermissible hindsight reconstruction and simply takes the inventor's disclosure as a blueprint for piecing together the prior art in an effort to defeat patentability. (See In re Dembiczak, 50 U.S.P.Q.2d 1614 (Fed. Cir.1999)). Simply put, the motivation to combine references can not come from the

invention itself. (See In re Oetiker, 977 F.2d 1443, 1447, 24 USPQ2d 1443, 1446 (Fed. Cir.1992). As discussed above, the Office Action has admitted that Hartley et al. fails to teach a kit with, in relevant part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. The Office Action attempts to explain away such a lack of teaching by alleging on page 6, lines 15-21 that one of skill in the art would have been motivated to include the primer complexes disclosed by Van Gelder et al. in the kit of Hartley et al. The Office Action provides that one of skill in the art would have been motivated to include the primer complexes disclosed by Van Gelder et al. in the kit of Hartley et al. based on the statement in Van Gelder et al. that the kit containing the primer complexes can have a variety of uses. This allegation is made relying on the fact that each of the individual pieces were present at the time of the invention, with no citation to anywhere in any of the cited references to support that their combination was suggested or motivated. The Office Action fails to provide any evidence of where in Hartley et al. or Van Gelder et al. such a motivation, teaching, or suggestion to combine comes from. The currently claimed subject matter is the only blueprint for such a combination, and as described above the motivation to combine references can not come from the invention itself. (See In re Oetiker, 977 F.2d 1443, 1447, 24 USPQ2d 1443, 1446 (Fed. Cir. 1992). Applicants emphasize that prior to Applicants' work the claimed kits were unknown. Prior to Applicants' work, no one had obtained such kits.

Thus, the Examiner has not met his burden of establishing that Hartley et al. or Van Gelder et al. either alone or in combination, disclose or suggest each and every element of claims 34 and 39-44. Accordingly, Hartley et al. or Van Gelder et al. do not make obvious claims 34 and 39-44. Applicants respectfully request withdrawal of this rejection.

3. Claim 46 was rejected under 35 U.S.C. § 103(a), as being unpatentable over Hartley et al. (5,043,272) in view of Van Gelder et al. (5,891,636) as applied to claims 34 and 39-44 and in further view of Blanco et al. (Journal of Biological Chemistry, 1989, Vil. 264(15), pg. 8935-40). Applicants respectfully traverse this rejection.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

Applicant's first note that claim 46 properly depends from claim 34, and therefore by definition, comprises all the limitations of claim 34. As such, the arguments stated above in reference to claim 34 apply to claim 46 as well. The Office Action relies on Hartley et al. and Van Gelder et al. in the same way and for the same disclosure for which Hartley et al. and Van Gelder et al. were applied in the 35 U.S.C. § 103(a) rejection of claims 34 and 39-44. The Office Action further admits that neither Hartley et al. nor Van Gelder et al. specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement (See Office Action page 7, lines 5-6).

Blanco et al., which is cited for its disclosure that phage vphi 29 DNA polymerase is highly processive in the absence of any accessory protein and is able to produce strand displacement coupled to the polymerization process, fails to supplement the elements missing from Hartley et al. and Van Gelder et al.. As discussed above in connection with the rejection under 35 U.S.C. § 103(a), Examiner has not met her burden of establishing that Hartley et al. nor Van Gelder et al. either alone or in combination, disclose or suggest a kit for amplifying a target nucleic acid sequence, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. Thus, Hartley et al., Van Gelder et al., and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 46. Accordingly, Hartley et al., Van Gelder et al., and Blanco et al. do not make obvious claim 34. Applicants respectfully request withdrawal of this rejection.

A Credit Card payment in the amount of $225.00, representing the fee for a small entity under 37 C.F.R. § 1.17(a)(2), and a Request For Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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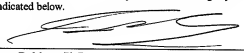

Scott D. Marty, Ph.D.

5-14-07
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